



Cofc

Attorney Docket No.: 9368-6IP

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Olmsted et al.

U.S. Patent No.: 6,783,939

Application Serial No.: 09/991,258

Issued: August 31, 2004

Filed: November 16, 2001

For: *Alphavirus Vectors and Virosomes with Modified HIV Genes for Use in Vaccines*

Date: November 9, 2006

Commissioner for Patents

Attn: Certificate of Correction Branch

P.O. Box 1450

Alexandria, VA 22313-1450

**REQUEST FOR CORRECTION OF ERRORS IN CERTIFICATE OF CORRECTION
ISSUED BY U.S. PATENT AND TRADEMARK OFFICE**

Sir:

It is respectfully requested that a new Certificate of Correction be issued for the above-identified patent in accordance with 37 C.F.R. § 1.322 to correct mistakes incurred by the United States Patent and Trademark Office (USPTO) in the Certificate of Correction issued on September 26, 2006. Enclosed is a copy of the original four page Certificate of Correction as issued by the USPTO, along with a copy of the originally filed Certificate of Correction, with errors on page 3 of the USPTO issued document highlighted and correct text on page 2 of the originally filed Certificate highlighted. Also enclosed is a new Certificate of Correction with bolded text on page 2 showing corrections to be made.

No fee is believed due. However, the Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account 50-0220.

Respectfully submitted,

Mary L. Miller

Mary L. Miller

Registration No. 39,303

**Certificate
NOV 15 2006
of Correction**

Myers Bigel Sibley & Sajovec, P.A.

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I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Attn: Certificate of Correction Branch, P.O. Box 1450, Alexandria, VA 22313-1450 on November 9, 2006.

Jessica M. French

Jessica M. French

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 6,783,939
DATED : August 31, 2004
INVENTOR(S) : Olmsted et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In the Claims:

Column 167, claim 1 should read -- 1. A composition comprising two or more isolated nucleic acids selected from the group consisting of an isolated nucleic acid encoding an *env* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, an isolated nucleic acid encoding a *gag* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and an isolated nucleic acid encoding a *pol* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof is modified to inhibit reverse transcriptase activity. --

Column 167, claim 2 should read -- 2. A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof is modified to inhibit reverse transcriptase activity. --

Columns 167-168, claim 3 should read -- 3. A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product or a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof is modified to inhibit reverse transcriptase activity, and wherein the alphavirus replicon particles comprise a replicon RNA or at least one structural protein which comprises one or more attenuating mutations. --

Column 168, claim 7 should read -- 7. A composition comprising two or more isolated nucleic acids selected from the group consisting of an isolated nucleic acid encoding an *env* gene product a fragment containing an epitope thereof of a human immunodeficiency virus, an isolated nucleic acid encoding a *gag* gene product a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and an isolated nucleic acid encoding a *pol* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of protease, integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof. --

Column 169, claim 8 should read -- 8. A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, or a fragment containing

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an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or the said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof. --

Column 169, claim 9 should read -- **9.** A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of protease, integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof, and wherein the alphavirus replicon particles comprise a replicon RNA or at least one structural protein which comprises one or more attenuating mutations. --

Column 169, claim 13 should read -- **13.** An isolated nucleic acid encoding a *pol* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, **wherein** the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof. --

Columns 169-170, claim 18 should read -- **18.** A method of making the alphavirus replicon particle of claim 17, comprising

- a) providing a helper cell for producing an infectious, defective alphavirus particle, comprising in an alphavirus-permissive cell:
 - (i) an alphavirus replicon RNA, wherein the replicon RNA comprises an alphavirus packaging signal and a nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of protease, integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof, and wherein the replicon RNA lacks sequences encoding alphavirus structural proteins;
 - (ii) a first helper RNA separate from said replicon RNA, said first helper RNA encoding at least one alphavirus structural protein and furthermore not encoding at least one other alphavirus structural protein; and
 - (iii) one or more additional helper RNA(s) separate from said replicon RNA and **separate from said first helper RNA, said additional helper RNA(s) encoding at least one other alphavirus structural protein not encoded by said first helper RNA;**
- and with at least one of said helper RNAs lacking an alphavirus packaging signal;
- wherein the combined expression of the alphavirus replicon RNA and the helper RNAs produces an assembled alphavirus replicon particle which is able to infect a cell, and is unable to complete viral propagation, and further wherein the population contains no detectable replication-competent alphavirus particles as determined by passage on permissive cells in culture;
- (b) producing the alphavirus replicon particles in the helper cell; and
- (c) collecting the alphavirus replicon particles from the helper cell. --

MAILING ADDRESS OF SENDER:

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PATENT NO. 6,783,939

No. of additional copies: _____

This collection of information is required by 37 CFR 1.322, 1.323, and 1.324. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1.0 hour to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you are required to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Attention Certificate of Corrections Branch, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

COPY

PATENT NO. : 6,783,939
DATED : August 31, 2004
INVENTOR(S) : Olmsted et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In the Claims:

Column 167, claim 1 should read -- 1. A composition comprising two or more isolated nucleic acids selected from the group consisting of an isolated nucleic acid encoding an *env* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, an isolated nucleic acid encoding a *gag* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and an isolated nucleic acid encoding a *pol* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof is modified to inhibit reverse transcriptase activity. --

Column 167, claim 2 should read -- 2. A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof is modified to inhibit reverse transcriptase activity. --

Columns 167-168, claim 3 should read -- 3. A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product or a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof is modified to inhibit reverse transcriptase activity, and wherein the alphavirus replicon particles comprise a replicon RNA or at least one structural protein which comprises one or more attenuating mutations. --

Column 168, claim 7 should read -- 7. A composition comprising two or more isolated nucleic acids selected from the group consisting of an isolated nucleic acid encoding an *env* gene product a fragment containing an epitope thereof of a human immunodeficiency virus, an isolated nucleic acid encoding a *gag* gene product a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and an isolated nucleic acid encoding a *pol* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of protease, integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof. --

Column 169, claim 8 should read -- 8. A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, or a fragment containing

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COPY

an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or the said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof. --

Column 169, claim 9 should read -- 9. A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of protease, integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof, and wherein the alphavirus replicon particles comprise a replicon RNA or at least one structural protein which comprises one or more attenuating mutations. --

Column 169, claim 13 should read -- 13. An isolated nucleic acid encoding a *pol* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof. --

Columns 169-170, claim 18 should read -- 18. A method of making the alphavirus replicon particle of claim 17, comprising

- a) providing a helper cell for producing an infectious, defective alphavirus particle, comprising in an alphavirus-permissive cell:
 - (i) an alphavirus replicon RNA, wherein the replicon RNA comprises an alphavirus packaging signal and a nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of protease, integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof, and wherein the replicon RNA lacks sequences encoding alphavirus structural proteins;
 - (ii) a first helper RNA separate from said replicon RNA, said first helper RNA encoding at least one alphavirus structural protein and furthermore not encoding at least one other alphavirus structural protein; and
 - (iii) one or more additional helper RNA(s) separate from said replicon RNA and separate from said first helper RNA, said additional helper RNA(s) encoding at least one other alphavirus structural protein not encoded by said first helper RNA;
- and with at least one of said helper RNAs lacking an alphavirus packaging signal;
- wherein the combined expression of the alphavirus replicon RNA and the helper RNAs produces an assembled alphavirus replicon particle which is able to infect a cell, and is unable to complete viral propagation, and further wherein the population contains no detectable replication-competent alphavirus particles as determined by passage on permissive cells in culture;
- (b) producing the alphavirus replicon particles in the helper cell; and
- (c) collecting the alphavirus replicon particles from the helper cell. --

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UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 6,783,939 B2
APPLICATION NO. : 09/991258
DATED : August 31, 2004
INVENTOR(S) : Olmsted et al.

Page 1 of 4

COPY

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In the Claims:

Column 167, claim 1 should read -- 1. A composition comprising two or more isolated nucleic acids selected from the group consisting of an isolated nucleic acid encoding an *env* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, an isolated nucleic acid encoding a *gag* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and an isolated nucleic acid encoding a *pol* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof is modified to inhibit reverse transcriptase activity. --

Column 167, claim 2 should read -- 2. A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof is modified to inhibit reverse transcriptase activity. --

Columns 167-168, claim 3 should read -- 3. A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product or a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof is modified to inhibit reverse transcriptase activity, and wherein the alphavirus replicon particles comprise a replicon RNA or at least one structural protein which comprises one or more attenuating mutations. --

Column 168, claim 7 should read -- 7. A composition comprising two or more isolated

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COPY

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 168, (cont'd)

nucleic acids selected from the group consisting of an isolated nucleic acid encoding an *env* gene product a fragment containing an epitope thereof of a human immunodeficiency virus, an isolated nucleic acid encoding a *gag* gene product a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and an isolated nucleic acid encoding a *pol* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion of inactivation of protease, integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof. --

Column 169, claim 8 should read -- 8. A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or the said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of integrase, RNase H and reverse transcriptase function in the *pol* gene product or said fragment thereof. --

Column 169, claim 9 should read -- 9. A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of protease, integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof, and wherein the alphavirus replicon particles comprise a replicon RNA or at least one structural protein which comprises one or more attenuating

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Page 1

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Column 169, claim 9 (cont'd)
mutations. --

Column 169, claim 13 should read -- 13. An isolated nucleic acid encoding a *pol* gene product or a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof. --

Columns 169-170, claim 18 should read -- 18. A method of making the alphavirus replicon particle of claim 17, comprising

a) providing a helper cell for producing an infectious, defective alphavirus particle, comprising in an alphavirus-permissive cell:

(i) an alphavirus replicon RNA, wherein the replicon RNA comprises an alphavirus packaging signal and a nucleic acid encoding a *pol* gene product, or a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or said fragment thereof comprises a modification resulting in deletion or inactivation of protease, integrase, RNase H and reverse transcriptase functions in the *pol* gene product or said fragment thereof, and wherein the replicon RNA lacks sequences encoding alphavirus structural proteins;

(ii) a first helper RNA separate from said replicon RNA, said first helper RNA encoding at least one alphavirus structural protein and furthermore not encoding at least one other alphavirus structural protein;
and

(iii) one or more additional helper RNA(s) separate from said replicon RNA and *separate from said first helper RNA, said additional helper RNA(s) encoding at least one*

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INVENTOR(S) : Olmsted et al.

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Columns 169-170, (cont'd)

other alphavirus structural protein not encoded by said first helper RNA;
and with at least one of said helper RNAs lacking an alphavirus packaging signal;
wherein the combined expression of the alphavirus replicon RNA and the helper RNAs
produces an assembled alphavirus replicon particle which is able to infect a cell, and is
unable to complete viral propagation, and further wherein the population contains no
detectable replication-competent alphavirus particles as determined by passage on
permissive cells in culture;

- (b) producing the alphavirus replicon particles in the helper cell; and
- (c) collecting the alphavirus replicon particles from the helper cell. --

Signed and Sealed this

Twenty-sixth Day of September, 2006



JON W. DUDAS

Director of the United States Patent and Trademark Office